Production and Application of Biodegradable Nanofibers Using Electrospinning Techniques

Tomasz Blachowicz and Andrea Ehrmann

Abstract Electrospinning is a versatile method to produce nanofibers or nanofiber mats from diverse polymers or polymer blends. Including ceramic or metallic nanoparticles can even be used to create purely inorganic nanofibers for diverse applications. On the other hand, biocompatible and biodegradable polymers are of high interest especially for biomedical applications. Biodegradable nanofiber mats as scaffolds can be used in tissue engineering, especially when degradation times are in the same order of magnitude as cell proliferation on these substrates. Biodegradation, however, involves more aspects than the pure time profile. Especially for utilization in vitro and in vivo, byproducts of degradation processes may lead to undesired reactions with the surrounding tissue, and vice versa. Here, we give an overview of the production techniques of biodegradable nanofibers and nanofiber mats by different electrospinning techniques. In addition, we report on biotechnological and biomedical applications of such fully or partly biodegradable nanofibers and show the chances and challenges in interaction with living tissue and organisms.

Keywords Electrospinning · Biodegradable nanofibers · Degradation processes · Biocompatibility · Biodegradability

1 Introduction

Electrospinning can be used to prepare fibers with diameters in a typical range of some ten to some hundred nanometers, sometimes up to the range of a few micrometers [1–3]. Due to their small diameter and the corresponding large surface-to-volume ratio, there are diverse applications of such nanofibers or nanofiber mats,

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for example, in the biomedical or biotechnological area [4–6], in filters [7–9], batteries, solar cells, and supercapacitors [10–12].

While nanofiber mats are often spun from polymers like polyacrylonitrile (PAN) and other petrochemical polymers [13–15], there are also diverse biopolymers which can be electrospun, e.g. proteins like gelatin [16], collagen [17], etc., polysaccharides like chitosan [18], cellulose [19], dextrose [20], etc., and diverse composites of two or more biopolymers as well as biopolymers blended with petrochemical polymers. While biopolymers generally stem from non-oil-based resources, here we have a deeper look into biodegradable polymers, i.e. polymers that are degraded by microorganisms or enzymes on time scales between hours and years [21]. Degrading means a high-molecular weight polymer is degraded into lower molecular weight fractions, in addition to modifications of CO_2 and oxygen content, finally resulting in a full collapse of the structure and the corresponding loss of the mechanical properties [22]. Especially in biomedical applications, biodegradable nanofibers are of high interest since they can be used for degradable implants, making surgical implant removal unnecessary; they are used in tissue engineering and similar life science applications [23].

This chapter is organized as follows: The next sub-chapter gives a short overview of biodegradation mechanism, followed by a sub-chapter describing possibilities to use typical biodegradable polymers for electrospinning, either solely or combined with a spinning agent which can be biodegradable or long-term stable. It should be mentioned that different biodegradable polymers show strongly different physical and chemical properties, which make the corresponding nanofibers highly interesting for different possible applications, of which several examples are given.

2 Biodegradation

Far more than 100 million tons of synthetic polymers worldwide are produced yearly, resulting in large amounts of household and industrial waste [24–26]. The idea of using biodegradable polymers is thus related not only to biomedical applications but also a reasonable method to reduce especially agricultural polymer waste [27]. Biodegradation means that microorganisms degrade a polymer, typically in the form of bacteria, fungi, and algae [28], by oxidation and hydrolysis to produce carbon dioxide, methane, and residual biomass as well as carbon in case of typical synthetic polymers, which is also converted into carbon dioxide [25–27]. While aerobic biodegradation, in the presence of oxygen, results in carbon dioxide production, anaerobic degradation mostly leads to methane production [29, 30].

Biodegradation of most synthetic polymers is complicated, but often nevertheless possible under well-suited conditions [31, 32]. Typical approaches to prepare such polymers are using synthetic polymers with special groups which are prone to hydrolytic microbial attack, biopolyesters which can be derived from bacterial sources, and mixing synthetic polymers with natural ones which can be easily degraded by microorganisms, such as starch [31–33].

It should be mentioned that biodegradation does not only mean that the final step, resulting in carbon dioxide, water, and some other byproducts but also that several smaller molecules are usually formed along the way [34]. For poly(lactic acid (PLA) and poly(glycolides) (PGA), e.g. the small molecule lactic acid and glycolic acid are formed [35], which must be taken into account if these materials are used as biodegradable screws fixing broken bones since biodegradation will make the surrounding of the treated bone area more acidic and can result in inflammations [36]. Neutralizing or at least reducing this effect belongs to the important topics of recent research on PLA implants [37–39].

Another important point to mention is related to the time scales and environmental requirements of biodegradation—some materials which are claimed to be biodegradable may necessitate years or longer for at least partial biodegradation, and in many cases highly specialized environments are required which cannot be reached, e.g. in the common compost [40–42].

3 Electrospinning

A large amount of natural and synthetic polymers has been made available for electrospinning, including many biodegradable and biocompatible polymers which are typically used for biomedical and biotechnological applications [43]. The electrospinning process generally uses a strong electric field to drag polymer droplets from a polymer solution or melt from an electrode to a counter electrode. The most common setup is based on a syringe which constantly ejects the polymer solution or melt through a needle into the electric field [44]. At the tip of the needle, a so-called Taylor cone is formed. If the surface tension is overcome by the applied electric field, the polymer is ejected from the tip, stretched and accelerated until it reaches the collector where polymeric nanofibers are deposited [45]. This short description already suggests that many parameters will influence fiber formation, including conductivity, surface tension, molecular weight, and viscosity of the spinning solution, dimensions of the electrospinning equipment and the applied electric field, as well as environmental conditions such as temperature and humidity in the spinning chamber [46]. Besides the needle-based electrospinning process, electrospinning can also be performed using wires (Fig. 1), rotating cylinders, or other shapes as ejecting electrodes [47–49]. Similarly, the substrates may be composed of different materials and show different shapes, including fast rotating electrodes which can be used to align the nanofibers [50–52].

3.1 Solvents

An important issue in electrospinning biodegradable polymers is related to the solvent used to prepare the spinning solution. Several polymers, such as poly(ethylene oxide)

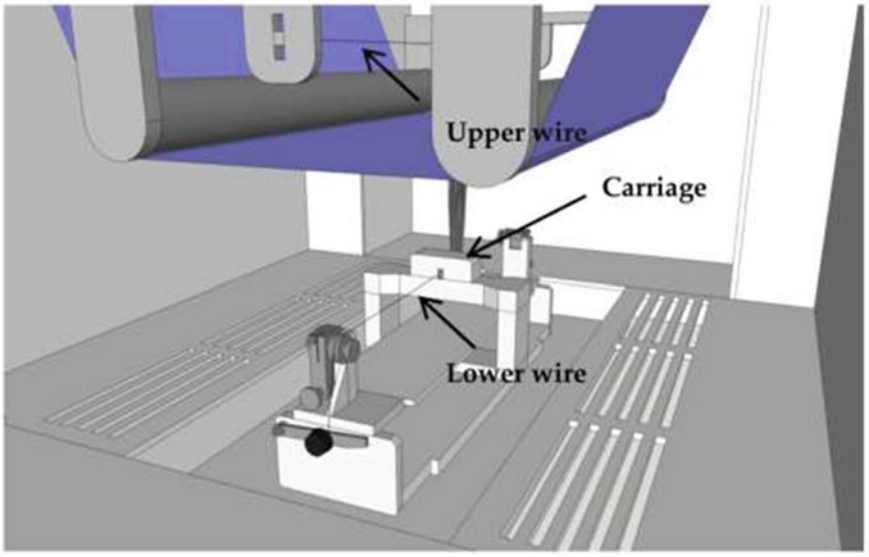

Fig. 1 Sketch of the Nanospider Lab, a commercially available equipment for wire-based electrospinning. From [47], originally published under a CC-BY license

(PEO) or gelatin, can be dissolved in water [53–55]. The disadvantage that the corresponding nanofiber mats can again be dissolved in water can be overcome by blending water-soluble and water-resistant polymers [56, 57] or by crosslinking the nanofiber mats after electrospinning [58–61].

On the other hand, some biodegradable polymers such as PLA need much more sophisticated solvents or solvent combinations to be electrospun. Septiyanti et al. reported recently on stereocomplex PLA, formed by solution blending poly(L-lactic acid) (PLLA) and poly(D-lactic acid) (PDLA) via electrospinning. While PLA is generally dissolvable in chloroform, they added N,N-dimethylformamide (DMF) to decrease the viscosity and hexafluoroisopropanol (HFIP) as a polar solvent with low surface tension to prepare thin fibers by needle-based electrospinning [62].

On the other hand, combining chloroform with a non-solvent of PLA such as dimethyl sulfoxide (DMSO) results in electrospinning of nanofibers with internal porosity, while surface porosity can be reached by adding ethanol to chloroform [63]. Blending PLA with ethylene vinyl acetate (EVA) was enabled using a solvent mixture from acetone and dichloromethane, resulting in electrospun nanofibers with good strength and flexibility [64]. Ghafari et al. tested solvent mixtures for electrospinning nanofiber mats from PLA, PEO, and cellulose and found that a chloroform/acetone/ethanol mixture showed a good dispersion of cellulose nanofibers and good electrospinnability of the polymer solutions. The resulting nanofiber mats also showed strong deviations, depending on the solvent mixtures, for example, of the mechanical properties and the water uptake [65]. While poly(vinyl alcohol) (PVA)

can be electrospun from an aqueous solution, poly [(R)-3-hydroxybutyrate-co-(R)-3-hydroxyhexanoate] (PHBH)/PVA nanofibers—which are interesting due to their high water uptake ability—can be electrospun using hexafluoroisopropanol (HFIP) or HFIP/water as solvent [66]. Hyaluronic acid is water-soluble, but belongs to the biopolymers that are usually claimed to be not electrospinnable solely due to the high electrical conductivity of the polymer solution, resulting in possible short-circuits between both electrodes [67]. Gelatin or another spinning agent was suggested to prepare corresponding blend fibers [68]. Nevertheless, some groups found possibilities not only to spin hyaluronic acid from sophisticated solution mixtures, such as distilled water/formic acid/DMF [69] or DMF/distilled water alkali solutions [70], but also by mixing water with the low-toxic dimethyl sulfoxide (DMSO) [71]. For a recent review on electrospinning hyaluronic acid, the reader is referred to [67]. A broad overview of possible solvent or solvent mixtures for electrospinning blends of natural and natural polymers is given in [72].

4 Biodegradable Natural and Man-Made Polymers

As mentioned before, biodegradable polymers are found among natural as well as man-made polymers. A brief overview of some of the most often used ones is given in Fig. 2 [72]. While biodegradation of the natural polymers occurs via the enzymatic route, by fungi, bacteria, etc. [73], hydrolytic biodegradation occurs in some of the synthetic polymers. Mechanical properties are on the average higher for the synthetic polymers, with exceptions such as the highly water-soluble PEO on the one side and the relatively strong silk fibroin on the other side. While natural polymers are usually hydrophilic, the hydrophobicity of the synthetic polymers depends on the material and can in some cases (e.g. polylactic-*co*-glycolic acid, PLGA) even be modified by chemical after-treatments. Electrospinning of these and some other interesting biodegradable polymers will be discussed in the next sub-chapters.

5 Electrospinning Biodegradable Polymers

5.1 Electrospinning Collagen

As the main protein of the extracellular matrix, collagen is of high interest for biomedical applications such as tissue engineering and drug delivery [74, 75]. To overcome the aforementioned weak mechanical properties of collagen nanofiber mats (Fig. 2), collagen is often blended with other natural or man-made polymers [76].

Most recently, Fahmi et al. prepared collagen/cellulose acetate (CA) electrospun nanofibers with embedded $MnFe_2O_4$ magnetic nanoparticles, enabling controlling the release of NAP under magnetic induction. They blended CA in acetone with

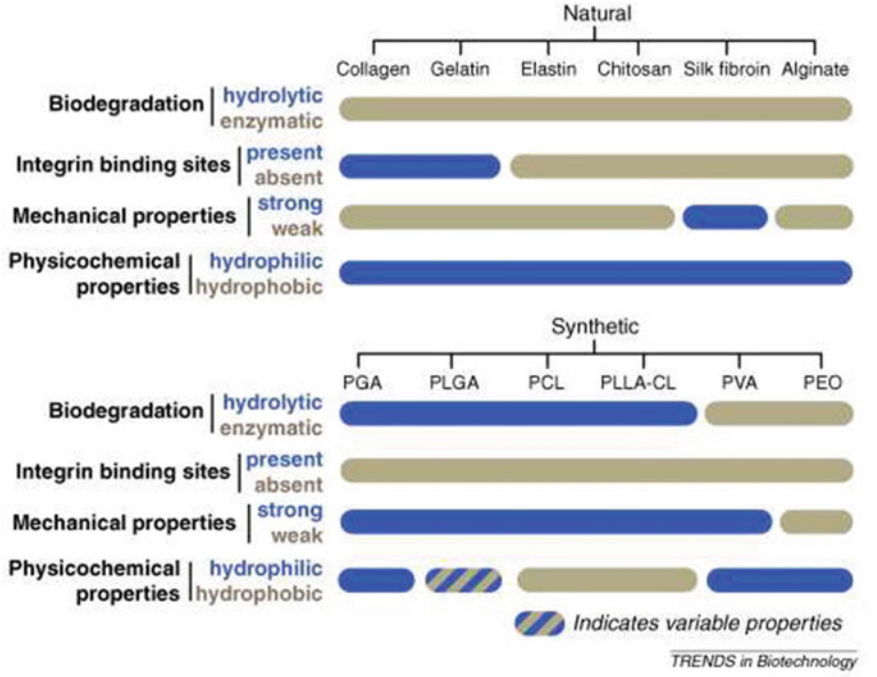

Fig. 2 Often used natural and synthetic biodegradable polymers with some physical, biological, and chemical properties. From [72], reprinted with permission from Elsevier

collagen dissolved in water to prepare a homogenous spinning solution in which the magnetic nanoparticles, dispersed in chloroform, as well as naproxen as a model drug, were added. This solution was electrospun using needle-based equipment and a cylinder collector, as depicted in Fig. 3, after optimizing the flow rate which was found to be critical for stable nanofiber formation [77].

Labbafzadeh et al. prepared polyvinyl alcohol (PVA)/collagen electrospun nanofibers with Fe_3O_4 (magnetite) nanoparticles for bovine serum albumin (BSA) release and also found a strong impact of an external magnetic field on the BSA release, enabling approximately one order of magnitude higher BSA release than without a magnetic field [17]. Combining collagen with polycaprolactone (PCL), Rather et al. prepared a drug-delivery scaffold for early osteogenic differentiation by needle-based electrospinning. Two supporting drugs were encapsulated in the electrospun nanofibers and slowly released for 4 weeks. While these drugs slightly influenced the fiber diameters, the general diameter distributions and morphologies showed high-quality fibers [78].

Blending Zein/PCL dissolved in chloroform/ethanol with collagen dissolved in ethanol resulted in spinning solutions with different amounts of collagen. Needle-based electrospinning resulted in different fiber morphologies, depending on the amount of collagen. These nanofibers could additionally be loaded with aloe vera and

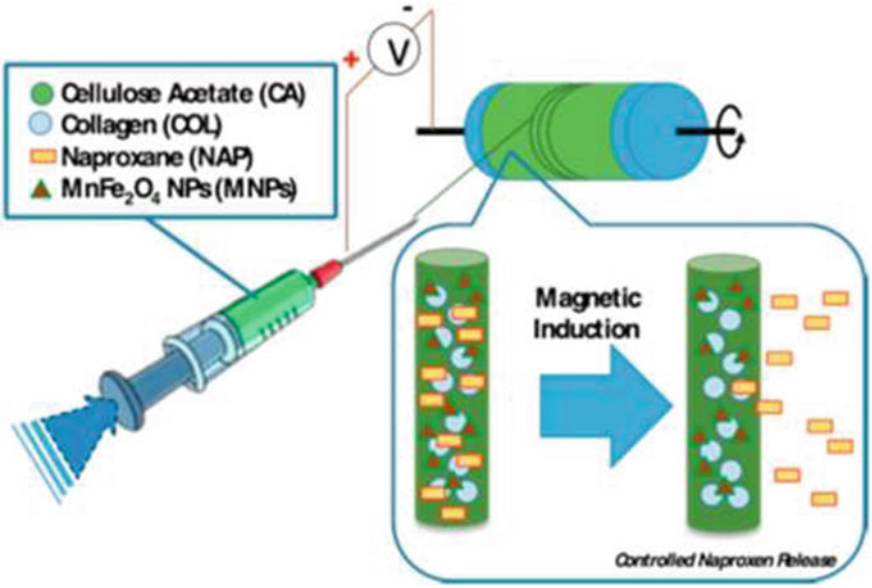

Fig. 3 Needle-based electrospinning of collagen/CA solution with additional magnetic nanoparticles and a model drug. From [77], reprinted with permission from Elsevier

ZnO nanoparticles for wound healing applications [79]. Gao et al. blended collagen type I in different weight ratios with cellulose diacetate-graft-poly(ethylene terephthalate), dissolved in HFIP, for needle-based electrospinning. The resulting nanofiber mats were crosslinked in glutaraldehyde vapor. While the mean fiber diameters and the water contact angles decreased with increasing collagen content, no significant differences were found in the mechanical properties. On the other hand, proliferation of bone marrow mesenchymal stem cells was supported by larger amounts of collagen [80]. Besides these few most recent studies on electrospinning collagen blends, only very few reports exist on electrospinning pure collagen. Most recently, Berechet et al. reported on electrospinning collagen hydrolysate, loaded with essential oils, with a needle-based technology [81]. Several other possibilities exist to combine nanofibrous structures with collagen, for example, by grafting collagen onto a nanofiber mat [82]. Here, however, these attempts are not further described.

5.2 Electrospinning Gelatin

Opposite to collagen, gelatin is more often electrospun purely. Santos de Oliveira et al. used photographic-grade gelatin for electrospinning in a wire-based setup from acetic acid aqueous solution (50 vol%) and crosslinked the nanofiber mats

in formaldehyde vapor for different durations. These nanofiber mats were investigated by scanning electron microscopy (SEM) and phase-contrast X-ray computed tomography at the nanoscale (nano-CT) (Fig. 4), showing the strong influence of the crosslinking duration on the nanofiber mat structure [83].

A gelatin inner layer, loaded with menthol, was embedded between Balangu seed gum outer layers in a fully electrospun sandwich structure. Without crosslinking, the menthol release was prolonged, as compared to the pure gelatin nanofiber mat. Nevertheless, it should be mentioned that here release occurred on an order of magnitude of 2 min, not during hours or days, as would be expected for crosslinked nanofiber mats [84]. Zhang et al. added gum Arabic to a gelatin electrospinning solution and found not only better electrospinning characteristics but also high thermal decomposition stability upon heating up to 250 °C due to electrostatic interactions and new hydrogen bonds between these materials [85]. Core–shell fibers with poly(lactic-co-glycolic acid) (PLGA) core and gelatin shell were prepared by co-axial electrospinning. Combining two such electrospun layers with an inner pure PLGA nanofiber

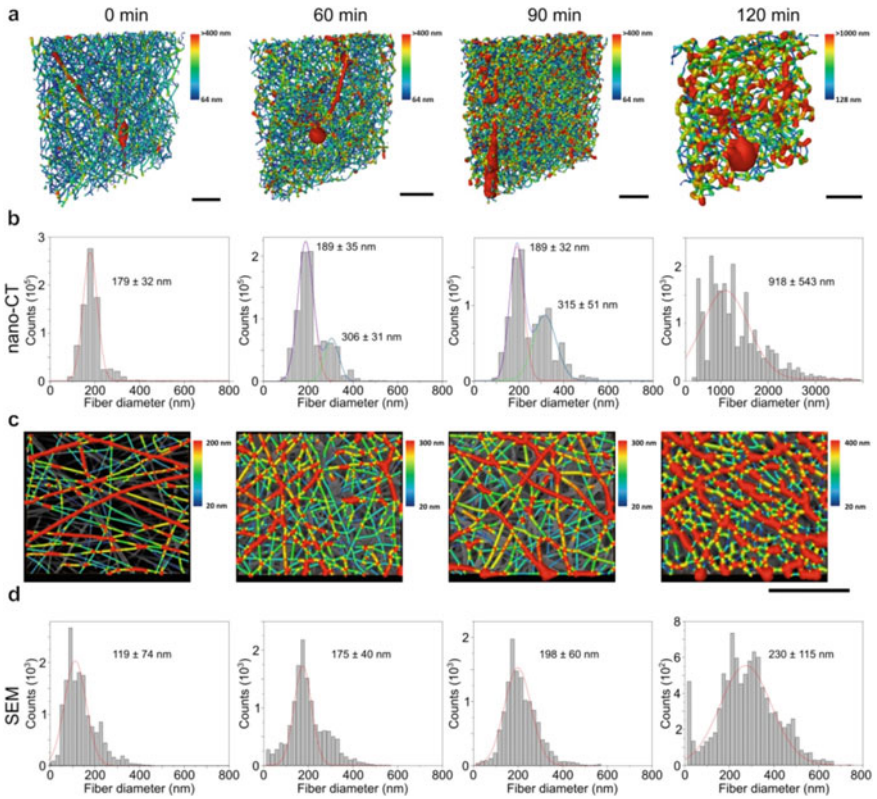

Fig. 4 Fiber characterization by **a** Nano-CT with colors encoding fiber thickness; **b** resulting fiber diameter distributions; **c** scanning electron microscopy images with color-coded fiber thickness; and **d** resulting fiber thickness. From [83], reprinted with permission from Elsevier

layer resulted in good mechanical strength, suture strength, and biocompatibility of this electrospun sandwich, making this approach useful for tissue engineering applications [86].

Besides such studies on pure and blended gelatin nanofibers, there are also attempts to use gelatin as a coating on nanofiber mats of different materials, for example, to improve the biocompatibility of the resulting structure. Du et al. produced calcium silicate nanofibers by electrospinning, followed by calcination at high temperatures between 800 °C and 1200 °C, and coated the resulting nanofiber mats with gelatin to improve their mechanical stability. By implanting these scaffolds in rat calvarial defects, new bone formation was shown [87]. As this brief overview of the most recent investigations in electrospinning gelatin shows, this material offers a broad variety of possible utilizations in electrospinning purely, in blends, sandwiches, or core–shell fibers.

5.3 Electrospinning Elastin

Elastin is only scarcely used in electrospinning. Since it belongs, together with collagen, to the main components of the extracellular matrix of the abdominal wall [88], it is nevertheless interesting for hernia repair and similar applications [89, 90]. On the other hand, elastin is insoluble since it contains crosslinked molecules between amino acid chains, making it necessary to hydrolyze the material before removing these crosslinked molecules [91]. Cao et al. dissolved different ratios of chitosan and elastin in a HFIP/acetic acid mixture for needle-based electrospinning. They found different fiber diameters, depending on the chitosan content, and increasing numbers of beads along the fibers for higher elastin content [92]. Adding elastin to PLGA electrospinning solution resulted in higher mechanical properties of the resulting nanofibers which supported the regeneration of epithelial organs [93]. Electrospun silk-elastin nanofiber mats showed good cytocompatibility and improved cell proliferation [94]. For dermal tissue engineering, human elastin/collagen composite scaffolds were electrospun, increasing cell migration and proliferation [95, 96]. Besides these interesting applications, studies on electrospinning elastin are rare.

5.4 Electrospinning Chitosan

In contrast to elastin, chitosan is often used purely or in blends with other materials. Nikbakth et al. loaded chitosan/PEO blend electrospun nanofibers with aloe vera for biomedical applications. They found the often occurring burst release within the first 5 hours, followed by a stain release over 30 h, and good biocompatibility [97]. For a completely different application, Surgutskaia et al. also used chitosan/PEO nanofibers. They modified chitosan with diethylenetriaminepentaacetic acid (DTPA), using different DTPA contents. DTPA is a chelating agent, forming stable complexes

with several metals, in this way supporting sorption properties of chitosan-based materials. As depicted in Fig. 5, the electrospun chitosan-DTPA/PEO was able to adsorb different metal ions after crosslinking in glutaraldehyde vapor [98].

Blending chitosan with PVA and encapsulating the antioxidant peptide ML11, Sannasimuthu et al. found increased wound healing activity in NIH-3T3 mouse embryonic fibroblast cells [99]. Mojaveri et al. also applied chitosan/PVA hybrid electrospun nanofibers to load them with the probiotic Bifidobacterium animalis subsp. lactis Bb12 and the prebiotic inulin. They found a strongly increased survivability of the cells in gastric and intestinal fluids, showing that such nanofiber mats can be used for protecting living probiotics in functional food [100]. Core–shell fibers composed of curcumin loaded cyclodextrin-graphene oxide core and gallic acid loaded chitosan shell were coaxially electrospun for controlled release of both drugs, which showed higher anti-cancer, antioxidant, and antimicrobial activity as well as anti-inflammatory properties than fibers loaded with one of the drugs [101]. Chitosan/PEO/berberine blend nanofibers were prepared by electrospinning, resulting in uniform, bead-free biocompatible fibers with drug release properties which could effectively support wound healing [102].

Pure chitosan nanofibers were prepared by modification with the negatively charged surfactant sodium dodecyl sulfate and after-treated with hemoglobin protein, in this way preparing a biosensor for electrocatalytic monitoring of hydrogen peroxide [103]. Electrospinning chitosan fibers loaded with simvastatin, a restenosis prevention drug, on stents showed constant drug delivery and will be tested in vivo in a future study [104]. While this brief overview already shows the broad range of possible material blends and applications of electrospun chitosan and chitosan blend

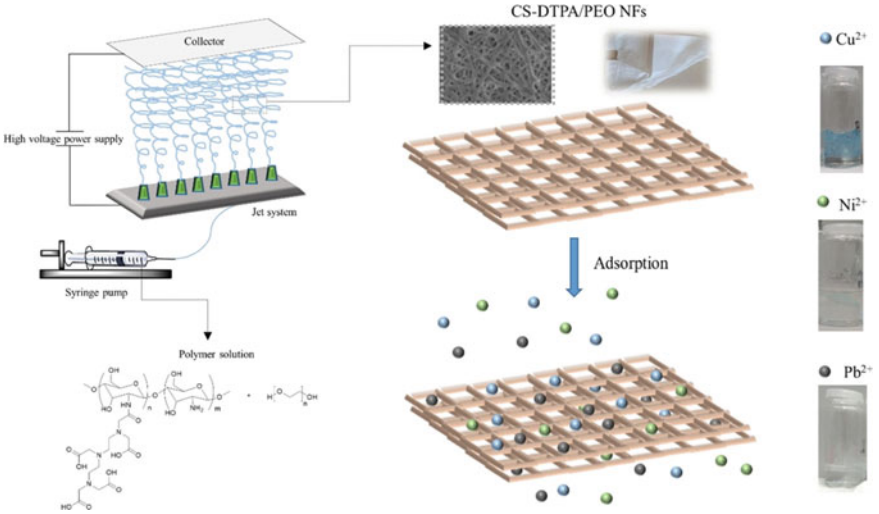

Fig. 5 Scheme of preparation and adsorption of chitosan-DTPA/PEO nanofiber mats. From [98], reprinted with permission from Elsevier

nanofibers, a comprehensive review of chitosan-based nanofiber mats with bioactive and therapeutic agents for would healing and skin regeneration can be found in [105].

5.5 Electrospinning Silk Fibroin

Natural silk has a fibrillary structure, with high elastic strength stemming from the silk fibroin protein [106]. Silk fibroin microparticles were electrospun, e.g. with poly(methylmethacrylate) (PMMA) and hyperbranched poly(ethyleneimine) (PEI) from DMF in different ratios. Mechanical tests showed a significant increase of the tensile stress of PMMA/PEI/silk fibroin nanofibers, as compared to pure PMMA nanofibers [107]. Silk fibroin was also electrospun blended with PCL and poly(glycerol sebacate) (PGS) from acidic solutions, resulting in good fibroblast attachment and growth of the resulting nanofiber mats [108]. To produce conductive silk fibroin nanofiber mats, Liu et al. embedded graphene into the spinning solution and produced highly aligned nanofibers by electrospinning to support cell adhesion and directional growth. They found an optimum balance between electrochemical and mechanical properties for a graphene content of 3%, resulting in enhanced neurite elongation on the corresponding nanofiber mats, making them possible candidates for electrically active scaffolds for neural regeneration [109]. Pure silk fibroin was electrospun, using silk from the mulberry silkworm *Bombyx mori*, by degumming the materials and dissolving it. By using high concentrations of 40–50 wt%, straight nanofibers could be spun from the pure silk fibroin, showing full biocompatibility [110]. Besides the aforementioned applications, silk fibroin nanofibers can also be used for drug delivery. A recent review on this possible application of silk fibroin electrospun nanofibers is given in [111].

5.6 Electrospinning Alginate

Alginate also belongs to the biopolymers which are often used in electrospinning. Alginate nanofibers can, for example, be used to encapsulate probiotic bacteria, similar to the aforementioned chitosan. As depicted in Fig. 6, *Lactobacillus paracasei* KS-199 was encapsulated in electrospun alginate nanofibers. The aqueous spinning solution was prepared from PVA/sodium alginate since pure alginate has a high conductivity and surface tension and is thus poorly electrospinnable. Electrospinning was performed using a needle-based system, followed by drying the nanofiber mats. While the pure spinning solution resulted in bead-free, smooth nanofibers, beaded nanofibers were created by adding the probiotic bacteria in which the viability of the cells was significantly increased under gastrointestinal conditions, as compared to free cells [112].

Similarly, Aloma et al. used PVA as a spinning agent for alginate, also resulting in nanofiber mats with good tensile strength and elongation properties, making

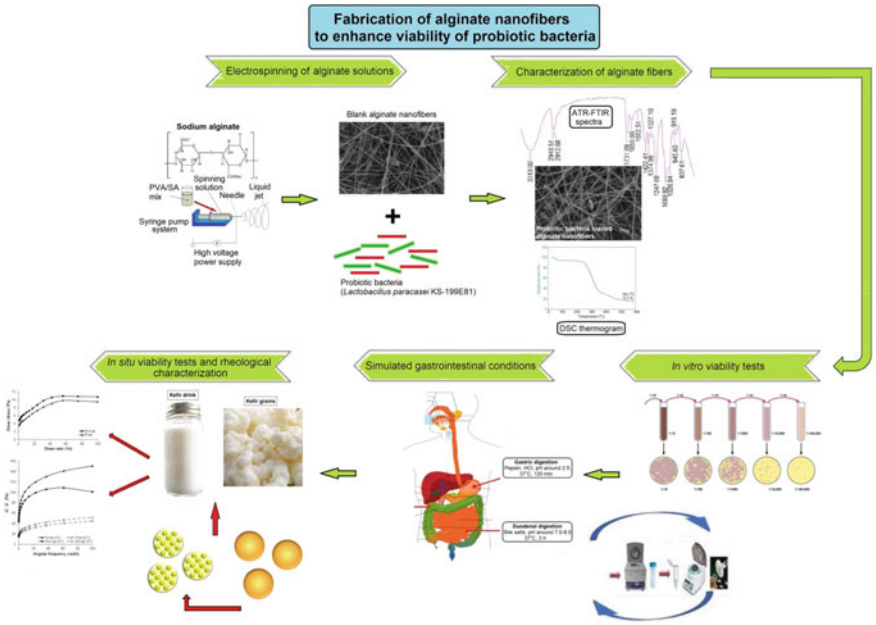

Fig. 6 Preparation of alginate nanofibers mats, loading them with probiotic bacteria and determining their effects to increase viability. From [112], reprinted with permission from Elsevier

them useful for wound dressings [113]. Najafiasl et al. added dexpanthenol to the PVA/sodium alginate core of electrospun nanofibers, while different shells enabled drug release control [114]. Another possible spinning agent for alginate is PEO. Gutierrez-Gonzales et al. loaded sodium alginate/PEO electrospun composites with curcumin and crosslinked the nanofiber mats with trifluoroacetic acid (TFA). Due to the resulting good mechanical properties, such nanofiber mats could be used for filters, tissue engineering, or food packaging [115]. Cesur et al. used PLA as spinning agent to prepare nanofibers for biomedical applications [116], while Amjadi et al. prepared zein/sodium alginate nanofibers for food packaging [117]. Rashtchian et al. applied alginate/PCL blends for electrospinning in which additional cellulose nanocrystals were embedded to increase the bio-mechanical properties [118]. As these few most recent examples show, alginate can be electrospun in blends with diverse other polymers, allowing for using the material in a broad range of applications.

5.7 Electrospinning Poly(Glycolic Acid) (PGA)

Opposite to the previously mentioned polymers, PGA is a synthetic biodegradable polymer. Being the simplest linear polyester, it is a semi-crystalline thermoplastic.

Although widely used in tissue engineering and regenerative medicine, PGA is only scarcely electrospun. In a blend with the aforementioned silk fibroin, Kim et al. used PGA as scaffolds for regeneration of rabbit calvarial defects, similar to the aforementioned procedure using gelatin-based scaffolds. Here, attachment and proliferation of pre-osteoblasts on a PGA and PGA/silk fibroin scaffolds were examined, showing better regeneration support of the hybrid scaffolds, making this material combination promising for guided bone regeneration and tissue regeneration [119]. A triple-blend of PGA with collagen and bioglass was used to prepare nerve guidance channels by electrospinning. This composite structure showed better mechanical, chemical, biocompatible, and biodegradable properties than pure PGA or PGA/collagen guidance channels and is thus promising for nerve regeneration [120]. Another possible blend partner for PGA is PEO. Electrospun PEO microparticles were used to increase the porosity of electrospun PGA and other biodegradable polymers, resulting in increased cell proliferation and human fibroblast infiltration, as compared to pure electrospun nanofiber mats, while the mechanical properties remained nearly unaltered [121]. PGA can also be blended with PCL for electrospinning. Loading these blended nanofibers with curcumin and polyhexamethylene biguanide (PHMB) as bactericides resulted in a strong drug release dependence on the PGA/PCL ratio, while generally showing a bactericide effect in hydrophilic and hydrophobic environments [122]. Finally, it should be mentioned that adding TiO_2 to electrospun PGA nanofibers was used as a degradation retardant for low-molecular-weight PGA. Interestingly, TiO_2 in the hygroscopic anatase modification was found to be a more efficient hydrolytic degrader than TiO_2 in the rutile modification [123].

5.8 Electrospinning Poly(Lactic-Co-Glycolic Acid) (PLGA)

Shen et al. used the copolymer of PLA and PGA, PLGA, as the core of electrospun nanofibers, surrounded by a shell of chitosan with acid-neutralizing capability to avoid the aforementioned acidic degradation products after implantation and found indeed that the pH decrease during degradation of the PLGA core was hindered [124]. PLGA was blended with gelatin to prepare nanofibrous tubular scaffolds with inner and outer layers of fibers with PLGA-core and gelatin shell, separated by a PLGA nanofiber layer, mimicking native vascular structures for cardiovascular tissue engineering. By this sandwich structure, mechanical strength, suture strength, and biocompatibility against human umbilical vain endothelial cells could be improved [125]. Blending PLGA with PCL was used to produce electrospun nanofibers as stent coatings, in order to block the flow toward the aneurysm cavity while allowing nutritional support to the vessel. This nanofiber coating resulted in improved physicochemical and mechanical properties, while it was bioabsorbable [126]. As described before for PGA, PLGA can also be used for guided bone regeneration. Dos Santos et al. used bilayer membranes of a dense PLGA layer doped with hydroxyapatite (HAp) on which PLGA blended with different amounts of HAp:beta-tricalcium phosphate was electrospun, resulting in a dense layer pore size of ~4 μm and a

high degree of porosity of the electrospun layer, preventing fibroblast infiltration, but enabling osteoblast migration and nutrient permeation. The combination with calcium phosphates resulted in improved osteoblast attachment, proliferation, and migration, making this system promising for bone reconstruction [127]. A completely different application was chosen by Zheng et al. who blended the piezoelectric PLA with the non-piezoelectric, but faster degradable PLGA in different ratios. By adding additional magnetic nanoparticles, the possibility was examined to control piezoelectricity magnetically. In this way, a potential magneto-electric nanocomposite for biomedical applications was prepared [128].

5.9 Electrospinning Polycaprolactone (PCL)

PCL is an often used polymer in biomedical applications. Rostami et al. used PCL/graphene oxide (GO) nanocomposites loaded with osteogenic drugs as scaffolds to increase the osteogenic differentiation of mesenchymal stem cells. Adding GO and osteogenic drugs resulted in improved hydrophilicity, cell viability and osteogenic differentiation, as compared to pure PCL scaffolds, making these nanocomposites promising for bone tissue engineering applications [129]. Bone regeneration was also the target of a study by Sruthi et al., using coaxial electrospinning to produce PCL/polyvinylpyrrolidone (PVP) fibers with embedded chitosan nanoparticles, loaded with veratric acid. These nanofibers showed not only biocompatibility with mouse mesenchymal stem cells but also promotion toward osteoblast differentiation [130]. PCL electrospun nanofibers loaded with polyaniline (PAni) coated TiO_2 nanoparticles and the aforementioned restenosis prevention drug simvastatin enabled drug release control by the TiO_2/PAni concentration, in this way stabilizing cell proliferation and attachment, as compared to pure PCL nanofibers [131]. One of the problems of PCL electrospun nanofiber mats for cartilage repair is their small pore size, combined with hydrophobicity, which prevents cell attachment and proliferation. Blending PCL with gelatin introduces favorable biological properties. Additionally electrosprayed PEO particles, as described before, introduce increased pore sizes when these sacrificial particles are removed after electrospinning. In this way, cell attachment and proliferation could significantly be enhanced [16]. Another application of PCL/gelatin nanofiber mats can be found in wound healing. Jafari et al. found that double-layer electrospun nanofiber mats, including amoxicillin as a model drug in the upper layer and ZnO nanoparticles for increased wound healing in the bottom layer, showed sustained release of the model drug during 144 h, combined with hindered bacterial growth and accelerated cell proliferation. In vivo tests additionally revealed accelerated wound contraction and reduced scar formation, making this system also interesting for wound healing [132]. Similarly, zein/PCL/collagen nanofiber mats were found to support wound healing [79]. Besides these few mentioned examples, many more studies report on PCL as a typical material for wound healing, bone repair, soft tissue engineering, and other biomedical applications.

5.10 Electrospinning Poly(L-Lactide-E-Caprolacton) (PLLA-CL)

Only very few studies report on electrospinning PLLA-CL, a polymer prepared using the ring-opening polymerization of L-lactide and ε-caprolactone as monomers. Yin et al. used electrospun silk fibroin/PLLA-CL vascular grafts, loaded with growth factor, to grow smooth muscle cells. The growth factor resulted in deeper infiltration of the cells into the graft, as compared to the pure nanofiber mat, making this system promising for tissue-engineered blood vessels [133]. Block-copolymer PLLA-CL was tested for controlled drug release from electrospun nanofibers, embedding protein molecules in the core and PLLA-CL as well as PCL and PLLA as cores. Depending on shell material and concentration, different mechanical properties and drug release kinetics were found, showing a burst release followed by a controlled, constant release [134]. Huang et al. used electrospinning to prepare collagen/PLLA-CL nanofiber mats with sufficient mechanical strength and flexibility due to the PLLA-CL, while the collagen supported the biocompatibility of the composite scaffolds, indicating this system's potential for vessel repair [135].

5.11 Electrospinning PVA

PVA can, for example, be used for drug delivery. Li et al. loaded PVA nanofiber mats with finasteride, a drug for prostatic hyperplasia treatment, and stabilized the electrospun nanofiber mats by a heat treatment, resulting in increased crystallinity and thus improved water stability. These nanofiber mats showed good cytocompatibility and higher embolization efficacy, resulting in a stronger prostate volume reduction as compared to pure crosslinked PVA nanofibrous particles by combining physical embolization with localized medical therapy [136]. To improve the mechanical properties of PVA nanofiber mats, Choy et al. blended it with α-chitin, in this way increasing the stiffness by nearly a factor of 20 and the extensibility by nearly a factor of 4. At the same time, the thermal stability was increased, suggesting such molecular design approaches to improve the thermomechanical performance of electrospun nanofiber mats [137].

A completely different material mix was investigated by Chenari et al. who added CuO to PVA nanofibers and found varying physicochemical properties, depending on the heat treatment after electrospinning [138]. Adding propolis to PVA nanofibrous wound dressings, Alberti et al. investigated wound healing potential in vitro and in vivo, applying murine NIH-3T3 fibroblasts as model cells. While pure PVA scaffolds showed good fiber morphology and no cytotoxicity to fibroblasts, adding propolis furthermore increased the wound closure rate after 7 days significantly, making this material blend suitable for tissue regeneration [139].

While many applications of PVA are related to biomedicine, Elhami and Habibi used PVA/montmorillonite electrospun nanofiber mats as UV protection. By measuring the degradation of methylene blue dye, shielded by these nanofiber mats, the amount of UV protection was estimated [140]. A more basic investigation on the PVA nanofiber alignment reached by electrospinning on parallel electrode collectors was performed by Icoglu et al. They found increased fiber alignment for decreased tip-to-collector distance and decreased charge density [141]. As another application, air filtration should be mentioned. Li et al. produced PVA/zein nanofiber mats by electrospinning and found an effect of the zein content as well as the alcoholysis degree on the air filtration efficiency, allowing optimizing the filtration effect by tailoring these material properties [142].

5.12 Electrospinning PEO

As the last material in this chapter, PEO is briefly presented. PEO mostly serves as a spinning agent for diverse polymers which are not or hardly electrospinnable solely, e.g. for chitosan [97, 98, 102], alginate [115], and PGA [121]. Nevertheless, PEO can also be used, for example, to prepare nanofiber mats serving as solvent-free electrolytes including lithium salts for the use in Li-ion batteries [12, 143]. Combined with PAni, conductive PEO/PAni nanofibers were prepared using rotating drum electrospinning to prepare supercapacitor electrodes [144]. Finally, PEO can be used as sacrificial material, for example, by electrospraying to allow for preparing pores by diluting it out of the fibers [16, 121] or by electrospinning it together with metallic or semiconducting nanoparticles, such as SnO_2, followed by calcinating the fibers to obtain the pure metal or semiconductor nanofibers [145]. Table 1 summarizes advantages and disadvantages of the aforementioned biodegradable polymers.

6 Conclusion

Many different biodegradable polymers can be used for electrospinning, either purely or in combination with a spinning agent. Water resistance is problematic for some of them, often necessitating an additional crosslinking step before the electrospun nanofiber mats can be used for the desired applications. On the other hand, blending such polymers with water-resistant ones or using them only for fiber formation, followed by a calcination step, are other possibilities to deal with the water solubility of some of them. As the short excerpt of the recent literature, given in this chapter, already shows, a broad range of physical, chemical, and biological properties can be found in biodegradable polymers, often supportive for biomedical applications such as wound healing and tissue engineering, but sometimes also related to quite different fields of research, e.g. using magnetic fields to control properties of composites with magnetic nanoparticles. We hope that this overview will give the readers new ideas

Table 1 Advantages and disadvantages of different biodegradable polymers

Material	Advantages	Disadvantages
Collagen	Main protein of the extracellular matrix Can be used for drug delivery	Weak mechanical properties, thus has to be blended with other polymers
Gelatin	Can be electrospun solely	Low thermal decomposition stability Necessitates crosslinking
Elastin	One of the main components of the extracellular matrix of the abdominal wall	Insoluble, thus needs hydrolyzation before electrospinning
Chitosan	Can be electrospun solely Useful for wound healing, drug release, etc.	
Silk fibroin	High elastic strength Electrospinnable solely	
Alginate	Usable for encapsulation of bacteria, wound dressing, etc.	Poorly electrospinnable due to high conductivity and surface tension
Poly(glycolic acid)	Combined with silk fibroin usable for bone and tissue regeneration	Not much literature available on electrospinning the material
Poly(lactic-co-glycolic acid)	Usable for guided bone regeneration Stent coating to increase physicochemical and mechanical properties	
Polycaprolactone	Blended with diverse materials useful for drug delivery, bone tissue engineering, wound healing, etc.	Small pore size and hydrophobicity of pure material prevent cell attachment
PVA	Electrospinnable purely Usable for drug delivery, wound healing, UV protection, air filtration, etc.	
PEO	Spinning agent, for example, for chitosan, alginate or PGA Sacrificial material to prepare pores	

about possible solutions for their recent applications and stimulate further research on well-known and emerging fields of interest.

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